Water-Electrolyte Balance, Lipid and Protein Metabolism, and State of Cell Plasma Membranes during Experimental Bile Peritonitis

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The development of experimental bile peritonitis was accompanied by a variety of homeostatic changes. The disease is characterized by a specific clinical and laboratory syndrome.

Key Words: *bile peritonitis; electrolytes; urea; cholesterol; erythrocyte volume*

Bile peritonitis (BP) is a serious complication of various surgical procedures, including cholecystectomy and liver transplantation. The incidence of this disease markedly increases with age. In elderly people impaired reactivity and discoordination of nervous system activity [6] determine reduced pain sensitivity, suppression of systemic inflammatory response, and impairment in self-evaluation of the severity of their condition. These peculiarities determine relative high ratio of patients with complicated cholelithiasis. BP is the most severe complication of cholelithiasis. Difficulties in early diagnostics and treatment of patients with BP determine the necessity of studying its pathogenesis.

Here we studied water-electrolyte balance and protein and lipid metabolism in animals with experimental BP.

MATERIALS AND METHODS

Experiments were performed on 29 male outbred dogs weighing 16±2 kg. Each animal was examined twice: before (intact dogs) and 24 h after modeling of BP (main group).

The content of K^+, Na^+, and Cl^- in blood plasma was measured using an Easy Lyte Plus K/Na/Cl automatic analyzer. Erythrocyte count, hematocrit, and mean volume of erythrocytes were estimated on a Medonic 620 analyzer. Total protein content, concentrations of albumin, urea, creatinine, glucose, and total cholesterol, and activities of alanine transaminase (ALT), aspartate transaminase (AST), creatine phosphokinase (CPK), and alkaline phosphatase (AP) were assayed on a Cobas Myra biochemical analyzer. The concentration of β-lipoproteins was measured on a Cormay-Livia automatic analyzer. Plasma osmolarity was calculated by the equation: $OSM=2\times Na^+ + K^+ + glucose + urea$ [4].

The results were analyzed by Student's *t* test for dependent variables. The data were expressed as $M\pm m$ [5].

RESULTS

Exudate with bile admixtures (200-400 ml) was revealed in the peritoneal cavity during laparotomy and sanation surgery 24 h after BP modeling. Peritoneal membranes had dull surface and were covered with fibrin. Intestine loops were paretically widened and hyperemic. Peristaltic motility was absent. Intraoperative signs were typical of severe inflammation in the peritoneal cavity.

Serious hemoconcentration manifested in a significant increase in hematocrit and blood erythrocyte count 24 h after BP modeling ($p<0.001$ compared to intact dogs, Table 1).

An impressive body of evidence suggests that the concentrations of Na^+ and K^+ in the blood decrease during peritonitis [1,3]. Table 1 shows that the con-

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centrations of Na^+ ($p<0.01$) and Cl^- in the plasma 24 h after modeling of BP were lower than in intact animals ($p<0.001$). K^+ concentration tended to decrease to 4.55±0.09 *vs*. 4.78±0.14 mmol/liter in intact animals). The decrease in Na^+ concentration was probably determined, on the one hand, by changes in hormonal regulation, in particular, increased synthesis of vasopressin in response to pain, which contributes to accumulation of water in the organism [4], and on the other, by the transport of Na^+ ions into cells along the concentration gradient due to impaired barrier function of cell membranes.

The decrease in plasma chloride concentration can be explained as follows: inflammatory process is accompanied by fewer rise and dyspnea leading to hyperventilation and a shift in acid-base balance towards respiratory alkalosis [2].

Blood osmolarity is an important characteristic of the aqueous phase, which determines the intensity of water exchange between the vascular bed and tissue. Variations in this parameter considerably modulate the metabolism of water and electrolytes. Blood osmolarity in experimental animals 24 h after modeling of BP was much lower compared to intact dogs ($p<0.05$).

Another mechanism for hemoconcentration can be proposed according to which the decrease in plasma osmolarity induces fluid transport into cells along the concentration gradient. These changes are accompanied by an increase in the erythrocyte volume and hematocrit. A primary change is probably the impairment of cell membrane permeability, which results in diffusion of Na^+ along its concentration gradient. Under normal conditions Na^+ concentration in the blood and cell is 140 and 20 mmol/liter, respectively. Na^+ flow is followed by water influx into cells, which causes their swelling. Our assumption is confirmed by the results of measuring the mean volume of erythrocytes. This parameter in intact and treated animals (24 h after modeling of BP) was 64.11±0.93 and 67.95±1.51 fl, respectively ($p<0.05$).

We measured the content of some metabolites characterizing functional activity of the liver and kidneys. Blood urea concentration significantly increased 24 h after BP modeling ($p<0.001$). However, creatinine concentration remained practically unchanged under these conditions (Table 1).

Functional impairment of cell membranes in organs manifested in activation of some intracellular enzymes.

Activities of AST, ALT, AP, and CPK increased by 58, 157, 160, and 226%, respectively, 24 h after modeling of BP (Table 2). The increase in enzyme activity reflects destabilization of the barrier function of cell membranes in organs and tissues [8].

CPK activity increased to a greater extent compared to another "heart enzyme" AST. The data suggest that destabilization of myocyte membranes containing this enzyme is more pronounced under these conditions. Changes in CPK activity occurred before surgery and intraoperative damage to muscles. Therefore, activation of this enzyme was not associated with muscle injury. The increase in urea concentration reflected the intensity of catabolic processes in the organism (similarly to AST activity). Creatinine concentration characterized excretory function of the kidneys and remained unchanged under these conditions. The degree of lipid metabolism reflected synthetic activity of the liver and increased by 1.3-1.6 times.

TABLE 1. Changes in Some Parameters of Water-Electrolyte Balance and Protein Metabolism in Animals (*M*±*m*)

Parameter	Intact animals	24-h BP
Hematocrit, %	39.9±1.1	51.7±1.2***
Erythrocytes, 10^{12}/liter	6.24±0.18	8.08±0.19***
Na^+, mmol/liter	147.0±0.8	141.7±1.3**
Cl^-, mmol/liter	107.8±0.5	101.3±1.0***
Osmolarity, mosm/liter	306.8±4.0	297.8±6.8*
Urea, mol/liter	4.72±0.37	8.03±0.75***
Creatinine, mol/liter	90.9±4.5	96.2±9.3

Note. *$p<0.05$, **$p<0.01$, and ***$p<0.001$ compared to intact animals.

The molecular pathogenetic mechanism of peritonitis includes profound changes in blood plasma lipids [7]. Twenty-four hours after BP modeling the contents of cholesterol and β-lipoproteins increased to 4.42±0.22 mmol/liter ($p<0.01$) and 35.47±3.29 U ($p<0.001$), respectively. In intact animals these parameters were 3.69±0.19 mmol/liter and 13.82±1.27 U, respectively. The increase in cholesterol content reflects adequate response of the organism to extreme changes in the peritoneal cavity. Published data show that hypocholesterolemia is a reliable criterion of mortality in patients with intraabdominal infection [9].

Due to considerable activation of synthetic processes in the liver, hemoconcentration, and sharp activation of catabolic processes, the protein content, concentrations of albumin and globulin 24 h after BP mo-

TABLE 2. Changes in the Activity of Some Enzymes in Animals (U/liter, *M*±*m*)

Enzyme	Intact animals	24-h BP
AST	51.68±7.50	81.83±6.96*
ALT	50.38±6.25	129.63±15.46**
AP	105.02±15.34	273.39±25.82**
CPK	287.50±29.05	936.85±154.78**

Note. *$p<0.01$, and **$p<0.001$ compared to intact animals.

deling (70.67±1.69, 25.84±0.61, and 44.84±1.60 g/liter, respectively) insignificantly differed from those in intact animals (72.09±1.44, 27.25±0.69, and 44.84±1.55 g/liter, respectively, $p>0.05$).

Blood glucose level significantly decreased 24 h after BP modeling (2.08±0.29 *vs*. 3.55±0.42 mmol/liter in intact animals, $p<0.001$). These changes were determined by intensive catabolic reactions, rather than animal's starvation due to poor general condition. Food restriction triggers a variety of compensatory reactions in intact animals, which prevents the decrease in blood glucose level below 3.00 mmol/liter.

Our findings indicate that specific metabolic clinical and laboratory syndrome develops 24 h after BP modelling manifested in hemoconcentration, dyselectrolytemia, nonspecific hyperenzymemia, increase in the contents of urea, cholesterol, and β-lipoproteins, and intensification of carbohydrate metabolism. This laboratory syndrome reflects impairment of water-electrolyte balance, change in barrier function of cell membranes, and progression of metabolic dysfunction.

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